

anesthetic and the alkalinizing agent are provided to the bladder separately.

The Examiner objected to Claims 1 to 13, 15 and 16 under 35 U.S.C. 103(a) as being obvious over Higson et al. or Sethia et al. Higson et al. discloses the treatment of detrusor instability through the simultaneous administration of lignocaine solution and sodium bicarbonate solution (see Summary at top of page 1; page 500, lines 35 and 36 and page 501, lines 1 and 2). Higson et al. does not teach or suggest that the lignocaine solution and sodium bicarbonate solution may be administered separately to beneficial effect.

Sethia et al. discloses a comparison of treatment of detrusor instability through the administration of sodium bicarbonate only (see page 516, column 2, lines 18 to 20), and treatment through the administration of lignocaine hydrochloride in bicarbonate solution (see page 516, column 2, lines 22 to 26). Sethia et al. conclude that little effect on bladder capacity is observed from such a method of treatment (see p. 518, column 1, lines 9 to 21), as lignocaine and an alkalinizing agent produce opposing effects which mask each other. Hence, Sethia et al. teaches against treatment comprising the administration of an anesthetic and an alkalinizing agent.

Claim 1 as amended relates to a method of anesthetizing the bladder of a patient comprising administering a local anesthetic and an alkalinizing agent separately.

The method of the present invention involves providing the alkalinizing agent at a concentration sufficient to increase the pH of the bladder so that at least a portion of the local anesthetic is converted to its lipid soluble base

form. The base form of the local anesthetic precipitates out of solution, and is deposited on the bladder mucosa. The deposited local anesthetic is then well placed to dissolve in the bladder mucosal layer, and then diffuse into the bladder wall. This form of the drug is, therefore, highly absorbable by the bladder (see p. 9, lines 2 to 5 of the Application as filed). If the anesthetic and alkalinising agent are mixed prior to administration as taught by Sethia et al. and Higson et al., the anesthetic will be converted to its base form and will precipitate out of solution prior to administration. The administration of the anesthetic will then be problematic. Commonly used methods of administration will not be appropriate. Furthermore, if the solution is administered but the precipitate remains in the administration apparatus, the concentration of lidocaine administered will be severely reduced, leading to a severely reduced anesthetic effect.

The separate administration of the local anesthetic and alkalinizing agent to the bladder, thus clearly provides a very important, non-obvious technical effect. None of the prior art documents cited teach or suggest a method of anesthetizing the bladder comprising the separate administration of a local anesthetic and an alkalinizing agent. Neither do any of the cited documents disclose the problems associated with mixing of the anesthetic and alkalinizing agent prior to administration. Applicant submits that Claim 1, and dependent Claims 3 to 8 and 15 are novel and inventive over the cited prior art.

Claim 9 provides a pharmaceutical combination for anesthetizing a patient's bladder comprising a local anesthetic and an alkalinizing agent wherein the local anesthetic and the alkalinizing agent are maintained separately until instilled in the bladder. Applicant

submits that this Claim is novel and inventive over the cited prior art as the separate administration allows formation of the highly absorbable base form of the anesthetic. Mixing of the anesthetic and alkalinizing agent prior to administration causes the anesthetic to precipitate out of solution leading to problematic administration. Claims 10 to 13 are dependent on Claim 9 and therefore, applicant submits that these Claims are also novel and inventive over the cited prior art.

The Examiner objects to Claim 14 under 35 U.S.C. 103(a) as being obvious over Higson et al. or Sethia et al. in combination with Askin. Askin teaches the administration of lidocaine in the treatment of interstitial cystitis. Askin does not suggest the administration of an alkalinizing solution. Claim 14 has been amended, and now relates to a method of treatment comprising the steps of administering an anesthetic and an alkalinizing agent separately. Applicant submits that this Claim is inventive over the prior art as the separate administration of the anesthetic and alkalinizing solution allows formation of the highly absorbable base form of the anesthetic when *in situ*. Claim 16 is dependent on Claim 14 and so applicant submits that this Claim is inventive over the cited prior art.

The Applicant believes that the present amended Application is in a condition for allowance and issuance of the Patent is earnestly solicited.

Respectfully submitted,

RICHARD HENRY

Daniel A. Monaco

DANIEL A. MONACO

Registration No. 30,480

DRINKER BIDDLE & REATH LLP

One Logan Square

18th and Cherry Streets

Philadelphia, PA 19103-6996

Phone: (215) 988-3312

Fax: (215) 988-2757

Attorney for Applicant

VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

1. (amended) A method for anesthetizing the bladder of a patient in need thereof, comprising the step of providing a sufficient quantity of a local anesthetic and an alkalinizing agent to the bladder of said patient to anesthetize the bladder, said local anesthetic and said alkalinizing agent being provided to said bladder separately, said local anesthetic being provided as an aqueous solution, said alkalinizing agent being provided in sufficient quantity to raise the pH of the bladder to approximately the pKa of the local anesthetic to convert at least a portion of said local anesthetic to its base form.

14. (amended) A method for treating interstitial cystitis, comprising the steps of periodically administering to a patient in need thereof a sufficient quantity of a local anesthetic and an alkalinizing agent, said local anesthetic and said alkalinizing agent being provided to said bladder separately, said local anesthetic and alkalinizing agent being provided to the bladder of said patient to anesthetize the bladder, said local anesthetic being provided in an aqueous solution, said alkalinizing agent being provided in sufficient quantity to raise the pH of the bladder to approximately the pKa of the local anesthetic to convert at least a portion of said local anesthetic to its base form.